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GND

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Jan E. Schnitzer and Philip Oh		
Application No.:	09/208,195	Group:	1644
Filed:	December 9, 1998	Examiner:	P. Nolan
For:	IMMUNOISOLATION OF CAVEOLAE		

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, P.O. Box 2327, Arlington, VA 22202

on 9/9/02 Christina M Sweeney
Date Signature

Christina M Sweeney
Typed or printed name of person signing certificate

RESPONSE

Assistant Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

Sir:

This Response is being submitted together with a Request for Continued Examination (RCE) for the referenced patent application, and with a copy of an executed Declaration under 37 C.F.R. §1.131 of Jan E. Schnitzer, M.D. These documents are submitted in lieu of a Notice of Appeal.

Applicants' Attorney respectfully requests a two-month extension of time. A Petition for Extension of Time and the appropriate fee are being filed concurrently.

REMARKS

Claims 1-9, 11-17, 19-22, 24-25 and 27-30 are pending. Claims 27-30 have been withdrawn from consideration.

The remainder of the Remarks is set forth under appropriate headings in the order in which the issues were raised in that Office Action, for the convenience of the Examiner.

Summary of Invention

The invention is drawn to methods of producing purified caveolae, the methods including an immunoisolation step of incubating a sample containing plasma membranes with an antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae. The methods are simple and efficient means of producing purified caveolae which closely resemble caveolae in their native state (e.g., caveolae covered with the oligomeric structural cage of caveolin); the methods also minimize contamination and loss of molecules that dissociate from caveolae over time. Furthermore, the methods do not require perfusion of a tissue or coating of the plasma membranes with colloidal silica (described, for example, in US Patent 5,776,770), and thus allow a high level of flexibility of starting materials, as the methods can be used even for tissues or samples that cannot be perfused or coated with colloidal silica.

Rejection of Claims under 35 U.S.C. 112, first paragraph

The Examiner rejected Claims 1-9, 11-17, 19-22 and 24-25, stating that the Specification did not provide enablement for a monoclonal antibody which binds oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae other than CAV (mAb clone 2234). The Examiner emphasizes that the state of the art teaches unpredictability in the ability to create antibodies with the properties of monoclonal antibody CAV.

Applicant respectfully disagree with this assessment. Applicants' disclosure describes the use of one antibody, CAV, which is representative of a type of antibody with a specific characteristic, namely, the ability to bind oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae. The Specification describes experiments by which the ability of an antibody to bind to caveolin in its native state as an oligomeric structural cage surrounding intact caveolae can be determined (see, e.g., p. 13, line 11 *et seq.*). One of ordinary skill in the art, given the screening criteria and the description of the specific

characteristic of the antibody (i.e., the ability to bind oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae) in the Specification, as well as the methods of determining the binding characteristics of the antibody in the Specification, would be able to identify other antibodies having the desired characteristics with no more than routine experimentation.

The inability of other antibodies used in the experiments described in the disclosure, or described in Oh and Schnitzer, to bind to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, does not indicate that undue experimentation would be necessary to identify other antibodies having the desired characteristics. Rather, it indicates only that those antibodies described in the experiments in the disclosure lack this particular characteristic and that a different antibody having this characteristic should be used in the methods of the invention.

In view of these considerations, the claimed invention is enabled by the Specification.

Rejection of Claims under 35 U.S.C. §102(b)

Claims 1-4, 6, 11 and 14 have been rejected under 35 U.S.C. §102(b), because the Examiner contends that they are anticipated by Scherer *et al.* The Examiner states that Scherer *et al.* teach two monoclonal antibodies, including mAb 2234 (i.e., CAV antibody). In particular, the Examiner stated that Mab 2234 was used by Scherer *et al.* "to immunoisolate caveolae."

In order for a reference to anticipate claims, the reference must teach every aspect of the claimed invention either explicitly or impliedly (see M.P.E.P. § 2131). As discussed in detail in the accompanying Declaration under 37 C.F.R. §1.131 of Jan E. Schnitzer, M.D., immunoprecipitation of a protein, as described by Scherer *et al.*, differs significantly from immunoisolation of a complex organelle, as described in the present invention, not only in the goals of the processes and the steps used, but also in the ultimate product that is obtained..

Scherer *et al.* describe a method of immunoprecipitation of caveolin. Immunoprecipitation refers to separation, usually of a single protein (in this case, caveolin), from the environment in which it is found (here, from a cell lysate) using an antibody. In the immunoprecipitation described by Scherer *et al.*, the cells are lysed in the presence of detergent (see "*Immunoprecipitation*" discussion), which not only disrupts but also destroys membranes, and strips lipids as well as proteins from cellular components, thereby exposing caveolin and allowing the antibody to bind to it. Thus, the methods of Scherer *et al.* strip away both lipids

and other proteins attached to caveolin, disrupting the structure of the caveolae and thereby eliminating the possibility of isolating the caveolae themselves.

Immunoisolation, as described in the Specification, separates a whole, complex organelle (a caveola) from plasma membranes of a cell, using an antibody. In the immunoisolation methods of the invention, a sample comprising plasma membranes is used; these membranes must be present in order to perform the methods of isolating caveolae, as the caveolae are organelles that are an integral part of the membranes. The caveolae are then separated from the plasma membranes.

Thus, it can be seen that immunoprecipitation of caveolin, as described by Scherer *et al.*, differs significantly from immunoisolation of caveolae as described in the Specification. Scherer *et al.* do not teach isolation of caveolae, but only isolation of caveolin. In view of these considerations, Scherer *et al.* do not teach every aspect of the claimed invention either explicitly or impliedly, and the claimed invention is therefore not anticipated by the teachings of Scherer *et al.*

CONCLUSION

In view of the discussion presented above, the claims are in condition for allowance. Applicants respectfully request that the Examiner reconsider and withdraw all rejections.

If the Examiner believes that a telephone conversation would expedite prosecution, the Examiner is invited to contact Elizabeth W. Mata at (915) 845-3558. If Elizabeth W. Mata cannot be reached, the Examiner is invited to contact Doreen Hogle at (978) 341-0036.

Respectfully submitted,

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